Seeking Harmony in Risk Assessment: Key Role for the Mode of Action

Resha M. Putzrath
Health Science Coordinator
Risk Assessment Forum Staff
National Center for Environmental Assessment
(202) 564-3229
putzrath.resha@epa.gov

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Historic approaches to human health risk assessment vary depending on the health effect of concern (e.g., cancer differed significantly from non-cancer effects, such as reproductive effects). Procedures that are harmonized, biologically based, and dependent on data rather than defaults offer the potential advantages of a less fragmented, more integrated, and more biologically consistent approach to risk assessment. Thus, the concepts of risk assessment should be more easily explained to stakeholders, including the general public. Furthermore, similar to all improvements in the quality of cancer risk assessments and risk communication, the harmonization process should better inform Federal, State, and local decision makers.

Mechanistic research on modes of action (MOA) have established biological linkages between non-cancer and cancer responses. Building on prior efforts and recommendations, EPA's Risk Assessment Forum has been exploring methods for harmonization of approaches to human health risk assessment. This effort is intended to

- establish a set of core principles on harmonization;
- develop a consistent set of principles for drawing inferences from scientific information for risk assessment;
- address short-term issues to move away from traditional dichotomies (e.g., with regard to cross-species scaling and point of departure (POD) for low-dose extrapolation); and
- move forward on new science (e.g., by promoting incorporation of toxicokinetic and mode of action data).

Key issues are being evaluated in parallel. Examples include

- use of the Benchmark Dose (BMD) suite of curve-fitting models to determine the POD for both cancer and non-cancer effects in the absence of agent-specific models;
- examination of toxicokinetics, toxicodynamics, and information on key MOA precursors to improve the accuracy of the dose-response function and for interspecies extrapolation (i.e., to determine the human equivalent dose); and
- reconsideration of the interpretation of and values for uncertainty factors (UFs) that were established for the NOAEL/LOAEL method for use with the BMD method.